

A Comparative study on C-reactive protein and Serum Bilirubin level as a predictor of Perforation or Gangrene in Acute Appendicitis.

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Background: Acute appendicitis i.e. inflammation of vermiform appendix is one of the most common surgical emergency. Despite this accurate clinical diagnosis is difficult as sign and symptoms of various pathological conditions presenting with acute abdomen are similar.^[2] The incidence of appendicular perforation has been documented to be ranging from 13 to 37% among adults^[3,4]. Early diagnosis and prompt treatment of appendicular perforation/ gangrene is important to reduce associated complications and mortality rate. Reliable and valid specific markers for diagnosis of acute appendicitis and its complications has not yet clearly identified till date. Hence in this study we will co-relate the preoperative serum bilirubin and C-reactive protein level in predicting the appendicular perforation or gangrene following acute appendicitis.

Methods: The present study was conducted on 76 patients of acute appendicitis admitted in General surgery department of our institute between 1st December 2018 to 30th June 2020. Patients underwent surgical procedure and was classified into two groups on the basis of intraoperative findings Group A (uncomplicated acute appendicitis), Group B (perforated or gangrenous appendix/complicated acute appendicitis). Data regarding the preoperative Serum C reactive protein level and Serum bilirubin level were compared using chi square test between two groups. Sensitivity and Specificity of investigations were also calculated in predicting the perforation or gangrene in acute appendicitis. Area under the curve (AUC) analysis was also done.

Results: Sensitivity of serum CRP level for detecting complicated appendicitis (perforation/ gangrene) was higher (87.1%) as compared to serum bilirubin level (77.4%) whereas specificity of serum bilirubin level was (84.4%) and serum CRP level was (75.6%) but Area under the curve (AUC) analysis for serum CRP level was higher (0.873) as compared to serum bilirubin level (0.74).

Conclusion: Although both serum CRP level and total serum bilirubin both are useful markers for prediction of complicated appendicitis, serum CRP level was observed to be more sensitive and specific and a better predictor of perforation or gangrene in case of acute appendicitis and can help in improving the overall outcome of patient.

Keywords: Serum CRP level, Serum Bilirubin level, Acute Appendicitis, Sensitivity, Specificity

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I. Introduction

Acute appendicitis is one of the most common general surgical emergencies presenting with abdominal pain worldwide and the estimated risk of appendicitis in lifetime has been reported to be approximately 7–8%.^[20] The risk of appendicular perforation is variable but is about 2% at 36 hours and increases about 5% every 12 hours following the onset of acute appendicitis.^[1] Elevated serum bilirubin level are commonly observed in septic patients^[5,6] due to hyperdynamic circulation bacteria, its toxin, cytokines and ischemia due to decreased hepatic blood flow to the liver.^[7,8]

C-reactive protein is an acute-phase inflammatory protein, a highly conserved plasma protein having both proinflammatory and anti-inflammatory properties and was initially discovered in 1930 by Tillet and Francis while investigating the sera of patients suffering from the acute stage of Pneumococcus infection and was named for its reaction with the capsular (C)-polysaccharide of Pneumococcus.^[41] CRP is thought to act as a surveillance molecule for altered self and certain pathogens. This recognition provides an early defense and leads to proinflammatory signal and activation of the humoral, adaptive immune system. CRP binds to molecular groups found on a wide variety of bacteria and acts as an opsonin. CRP may also be important in the recognition of necrotic tissues and binds to apoptotic cells, protects the cells from assembly of the terminal complement components, and sustains an anti-inflammatory innate immune response.

Very high levels of CRP and bilirubin in patients with appendicitis indicate gangrenous, perforation or suppurative evolution of the disease, especially if it is associated with leukocytosis and neutrophilia^[10]. Hence in this study we will co-relate the preoperative serum bilirubin and C-reactive protein level in predicting the appendicular perforation or gangrene following acute appendicitis.

II. Methods

This prospective study was conducted in department of General surgery of our Institute on 76 patients of more than 14 years of age having acute appendicitis and underwent surgical procedure between 1st December 2018 to 30th June 2020, Patient were classified into two groups on the basis of intraoperative findings Group A (uncomplicated acute appendicitis), Group B (perforated or gangrenous appendix/complicated acute appendicitis). Data regarding the preoperative Serum C reactive protein level and Serum bilirubin level and other variables were documented and compared using chi square test. Sensitivity and Specificity of investigations were also calculated in predicting the perforation or gangrene in acute appendicitis. Area under the curve (AUC) analysis of Receiver Operating Characteristic (ROC) was also done.

III. Results

Out of the 74 patients studied, Mean age of patients presenting with acute appendicitis was 33.42±12.69 years (range- 15-70) and maximum patients belonged to 21 to 30 years of age group (34.2%). Male predominance was observed in present study with male: female ratio of 3.5:1. Intraoperative findings were suggestive of acute appendicitis with no complication in 45 (59.2%) patients cases whereas appendicular perforation and gangrene was observed in 26 (34.2%) and 5 s(6.6%) cases respectively. CRP was raised i.e. >10 mg/L in 87.1% cases with Complicated appendicitis compared to 24.4% cases with uncomplicated appendicitis. The observed association of CRP with Uncomplicated appendicitis and complicated appendicitis was statistically highly significant (p<0.01) Table 1.

Serum CRP level (mg/l)	Group A (Uncomplicated appendicitis)	Group B (Complicated appendicitis)
<10	34 (75.6)	4 (12.9)
>10	11 (24.4)	27 (87.1)
χ^2	28.8	
P value	0.001	

Table 1. Comparison of C reactive protein levels amongst patients with uncomplicated and complicated appendicitis

Serum bilirubin levels was raised in 77.4% cases with complicated appendicitis whereas in cases of uncomplicated appendicitis, it was raised in only 15.6% cases. Test of significance (chi square test) observed statistically highly significant association of serum bilirubin levels with appendicitis and its complications (p<0.01) Table 2.

Serum bilirubin level (mg/dl)	Group A (Uncomplicated appendicitis)	Group B (Complicated appendicitis)
<1.2	38 (84.4)	7 (22.6)
>1.2	7 (15.6)	24 (77.4)
χ^2	29.1	
P value	0.001	

Table 2. Comparison of Serum Bilirubin levels between uncomplicated and complicated appendicitis

Sensitivity of CRP for diagnosis of perforated/gangrenous appendicitis (87.1%) was higher as compared to that of serum bilirubin levels (77.4%) whereas specificity of serum bilirubin levels was higher (84.4%) as compared to specificity of CRP (75.6%). PPV and NPV of CRP was 71.1% and 89.5% whereas that of bilirubin was 77.4% and 84.4% respectively Table 3

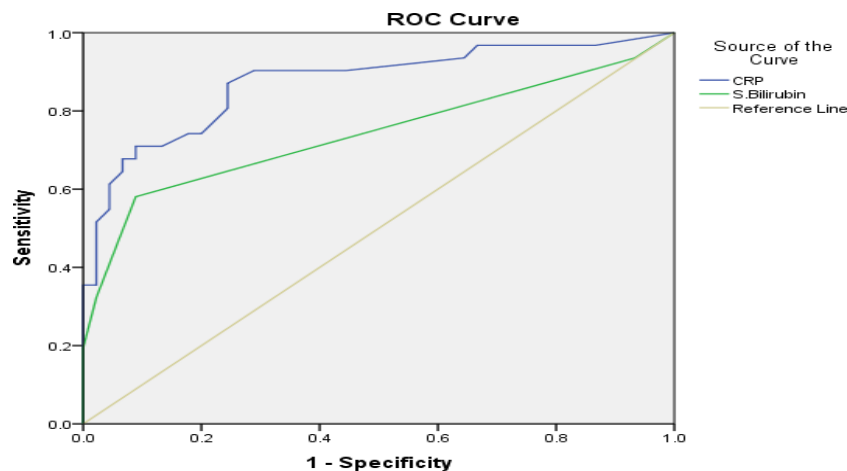
Diagnostic values	CRP level	Serum bilirubin level
Sensitivity	87.1	77.4
Specificity	75.6	84.4
PPV	71.1	77.4
NPV	89.5	84.4

Table 3. Diagnostic accuracy of CRP level and serum bilirubin level in prediction of perforation or gangrene in Acute Appendicitis

Above table represents that area under the curve for evaluating the diagnostic accuracy of CRP and serum bilirubin. It was observed that area under the curve was more for CRP (0.873) as compared to serum bilirubin (0.741), thus CRP is a better predictor of perforated/gangrenous appendicitis as compared to serum bilirubin levels Table 4

Area Under the Curve					
Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
S.CRPLLevel	0.873	0.044	0.001	0.787	0.959
S. BilirubinLevel	0.741	0.064	0.001	0.616	0.865

Table 4. Area under the curve for CRP level and Serum bilirubin levels



Diagonal segments are produced by ties.
Receiver operating curve for Serum CRP and Serum bilirubin level

IV. Discussion

In our study Serum CRP level was raised in 87.1% cases with complicated appendicitis when compared to 24.4% cases of uncomplicated appendicitis. Test of significance revealed statistically highly significant difference in mean Serum CRP levels in complicated appendicitis (28.90 ± 18.82 mg/L) as compared to uncomplicated appendicitis (8.13 ± 6.57 mg/L) (p value < 0.01). These findings were supported by study of Elgamal A Setal (2019) in which, CRP levels were higher in cases of complicated appendicitis and simple appendicitis as compared to normal appendix with significant differences ($P < 0.001$).^[11] This findings were also consistent with findings of Biradar N et al (2019) in which mean CRP levels were higher in appendicular perforation (1.8 ± 1.1 mg/dL) as compared to acute appendicitis (1.4 ± 0.5 mg/dL). Sensitivity of C-Reactive Protein (CRP) in predicting appendiceal perforation was 41.54%.^[12]

In present study serum bilirubin levels in complicated appendicitis was raised in 77.4% cases when compared to 15.6% cases of uncomplicated appendicitis. Also mean serum bilirubin levels were higher in complicated appendicitis i.e. 2.03 ± 1.25 mg/dL as compared to uncomplicated appendicitis (1.04 ± 0.47 mg/dL) ($p < 0.01$). This finding were supported by findings of Bali S et al (2020) in which out of 306 patients with perforated appendicitis, serum bilirubin was raised in 74% cases whereas out of 621 patients with uncomplicated appendicitis Elgamal AS et al (2019) also documented findings similar to present study i.e. high bilirubin levels in complicated appendicitis as compared to uncomplicated appendicitis ($p < 0.05$).^[11]

In present study, CRP was more sensitive (87.1%) but less specific (75.6%) as compared to bilirubin (sensitivity and specificity 77.4% and 84.4% respectively) for diagnosis of perforated or gangrenous appendicitis and the area under the curve was maximum for CRP (0.873) as compared to serum bilirubin (0.741). Pinate A Retal also observed almost similar sensitivity of raised CRP and total serum bilirubin levels for perforated appendix (i.e. 72.50% and 77.5% respectively).^[13] This findings were also supported by Wani MD et al findings of sensitivity and specificity of serum bilirubin for diagnosis of perforated appendicitis to be 78.6% and 89% whereas that of CRP level was documented to be 83% and 74% respectively.^[13] D'Souza N et al also documented higher specificity (82%) but lower sensitivity (70%) of serum bilirubin level for detection of perforated appendicitis as compared to CRP (21% and 80% respectively).^[14]

V. Conclusion

In our study we concluded that although both serum CRP and total serum Bilirubin levels are useful markers for prediction of complication in acute appendicitis. Serum CRP level was observed to be more specific and sensitive and a better predictor of perforation or gangrene in acute appendicitis when compared to serum bilirubin level. A study with a larger sample size and multiple centers is recommended to establish the same.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Ethics committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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